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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,171	08/31/2004	Kanako Suzuki	80179(302730)	5261

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EXAMINER	
HIBBERT, CATHERINE S	

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1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,171	SUZUKI ET AL.	
	Examiner	Art Unit	
	Catherine S. Hibbert	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *6* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,7-9,11,12 and 15-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7-9,11-12 and 15-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Upon careful reconsideration, the finality of the last Office action is withdrawn. Applicant's Amendments to the Claims filed 4 April 2008 are received and entered. Claims 4-6, 10 and 13-14 are cancelled. Claims 1-3, 7-9, 11-12 and 15-19 are pending and under examination in this action.

Response to Arguments

The rejection of claim 11 under ¶ 112(second paragraph) has been withdrawn based on Applicant's Amendments to the Claims.

The rejection of claims 1-3, 7, 11-12, and 15-19 under ¶ 102(b) as being anticipated by Boel et al has been withdrawn based on Applicant's Amendments to the Claims. The rejection of cancelled Claim 6 is moot.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 15-19 are newly rejected and Claims 7-9 stand rejected under 35 U.S.C. 102(b) as being anticipated by Minetoki et al [("Improvement of

promoter activity by the introduction of multiple copies of the conserved region III sequence, involved in the efficient expression of *Aspergillus oryzae* amylase-encoding genes" in Appl Microbiol Biotechnol, 1998:50 p.459-467, of record) for reasons of record and below. The rejection of cancelled claim 10 is moot.

Applicant's arguments filed 4 April 2008 have been fully considered but are respectfully not found persuasive.

Applicants response is to traverse the rejection under 102(b), as anticipated by Minetoki et al. because Applicants argue that the Minetoki et al. reference does not teach or suggest all the limitations of the instant claims. In particular, Applicants argue that the Minetoki et al. reference “does not teach or suggest a modified promoter constructed by inserting a first DNA fragment including CCAATNNNNNN (a first base sequence: SEQ ID NO: 1) and a second DNA fragment including GGNNNNNNNNNGG (a second base sequence: SEQ ID NO: 2) into a promoter, wherein the first DNA fragment and the second DNA fragment are combined as a pair, and in each pair, said first DNA fragment and said second DNA fragment are inserted so that they are arranged sequentially from the 5' end to the 3' end side of said promoter, according to the instant claims”. Applicants point to the examples in the instant application, “that show the enhanced promoter activity observed when inserting a first and second DNA fragment as a pair, as compared to a single fragment or a plurality of fragments”. For example, to support their argument, Applicants provide the following example from the instant specification, stating that

> enhancing the promoter activity by singly inserting CCAAT sequence or SRE was not observed...on the other hand, in the modified promoter (PSCP) in which a CCAAT sequence and SRE were inserted at the same time, as compared with the wild type promoter (taap), significant increase in the activity was observed, and about 4 times amylase' activity was observed. From the results, it can be said that in order to increase the promoter activity, it is important to insert both CCAAT sequence and SRE at the same time. (paragraphs [0099] and [0100] of the published application).

In addition, Applicants argue that the Minetoki et al. reference "merely teaches introducing multiple copies of the fragment comprising region III into the *Aspergillus* promoter (see, e.g.p.460, p.461, col. 1, p.464 col. 1)". Furthermore, Applicants argue that "nowhere does the Minetoki reference expressly or inherently teach or suggest the first DNA fragment and the second DNA fragment that are combined as a pair, and in each pair, said first DNA fragment and said second DNA fragment are inserted so that they are arranged sequentially from the 5' end to the 3' end side of said promoter, as instantly claimed".

Applicants' arguments have been fully considered but are respectfully not found persuasive because the instant claims are directed to a product and not to the process by which the product was made. The MPEP [2113 [R-1]] states that product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps". The MPEP states that

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even

though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

Claim 1 is directed to a modified promoter constructed by inserting a first DNA fragment including CCAATNNNNNN (a first base sequence: SEQ ID NO: 1) and a second DNA fragment including CGGNNNNNNNNNGG (a second base sequence: SEQ ID NO: 2) into a promoter wherein one first DNA fragment and one second DNA fragment are combined as a pair, and in each pair, said first DNA fragment and said second DNA fragment are inserted so that they are arranged sequentially from the 5' end to the 3'end side of said promoter, and wherein the modified promoter is capable of functioning in a filamentous fungus. In addition, the instant Claim 7 is drawn to the modified promoter of claim 1, wherein said first DNA fragment and said second DNA fragment are inserted at the 5'-end side that is upstream to a CCAAT sequence existing in said promoter or at the 3'-end side that is downstream to a SRE sequence existing in the promoter region.

Minetoki et al teach wherein a plurality of said first DNA fragments and a plurality of said second DNA fragments are inserted (claim 8), and further to wherein the same number of said first DNA fragments and said second DNA fragments are inserted (claim 9). For example, Minetoki et al teach modification of the promoter for the *Aspergillus oryzae* amyB gene (see title and abstract). Furthermore, Minetoki et al teach inserting multiple copies of Region IIIa sequence which contains the second base sequence "CGGAAATTTAAAGG"

inserted in tandem with the Region IIIb sequence which contains the first DNA fragment including the "CCAATNNNNNN" sequence into the promoter region of a modified vector (see especially Figure & legends 1 and 2). The sequence "CGGAAATTTAAAGG" also reads on a full-length SRE sequence (described above), which meets the limitations of Claim 7.

More specifically in response to Applicants arguments, the instant base claim 1, from which the instant claims 7-9 now depend, is drawn to wherein the first and second DNA fragment are inserted so that they are arranged sequentially from the 5'-end side to the 3'-end side of said promoter and that the Region IIIa taught by Minetoki et al represents the instant "second DNA fragment" while the Region IIIb taught by Minetoki et al represents the instant "first DNA fragment". However, Minetoki et al clearly teach wherein the multiple copies of the Region IIIa and IIIb are inserted into the promoter such that, for example, the following DNA fragments are arranged sequentially from the 5'-end side to the 3'-end side of said promoter: Region IIIa, Region IIIb, Region IIIa, Region IIIb, Region IIIa Region IIIb (see p.461, Figure 2). Therefore, the effect of the multiple copies of the Region IIIa and Region IIIb is that Region IIIb (the first DNA fragment) is actually arranged sequentially on both sides of the Region IIIa (the second DNA fragment). In addition, Claim 7 is directed to the modified promoter of claim 1, wherein said first DNA fragment and said second DNA fragment are inserted at the 3'-end side that is downstream to a SRE sequence existing in the promoter region. A broad, reasonable interpretation of an "SRE

sequence" could read on the nucleotide sequence "5'-ATTTAAAG-3'" which is contained in an SRE consensus sequence (see instant application Seq ID No. 6).

In addition, Minetoki et al teach using the modified promoter in the context of an expression vector (for example, the agdA gene is shown in page 463, Figure 5 as the target gene behind the modified promoter in the expression vector construct), and further teach the culturing the host fungus and collecting the produced enzyme protein (e.g. page 461, lines 6-10), which meets the limitations of Claims 15-19.

Therefore, the Minetoki et al reference meets all of the limitations of the instant claims 1, 7-9, and 15-19.

Claims 1, 15-19 are rejected and Claims 7-9 stand rejected under 35 U.S.C. 102(b) as being anticipated Minetoki et al for reasons of record and above. The rejection of cancelled claim 10 is moot.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 7, 11-12, and 15-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Minetoki *et al.*, as applied to claims 1, 7-9 and 15-19 above, and further in view of Boel et al (US Patent No. 5,536,661: issued 16 July 1996, of record).

Initially, it is noted that the instant claims are directed to a product and not to the process by which the product was made. The MPEP [2113 [R-1]] states that product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps". The MPEP states that

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The

patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

Claims 1, 7-9 and 15-19 are taught by Minetoki *et al*. for the reasons above.

However, Minetoki *et al*. differs from the invention claimed in the instant Claims 2-3, and 11 in that while it teaches the generic sequences of Claim 1 (i.e. SEQ ID NO:1-2), used as a modified promoter for the *Aspergillis oryzae* taka-amylase gene, Minetonka *et al*. fails to teach the specific species of SEQ ID NO: 3-4 and 9) (instant Claims 2-3, and 11). Minetoki et al also differs in the instant Claim 12 in that although it contemplates using the amyB promoter (also called TAKA-amylase promoter) in future studies, it does not explicitly use the amyB promoter in the study of reference.

Boel et al teach the use of the SEQ ID NO: 3-4 and 9 and explicitly uses the TAKA-amylase (*amyB)* promoter in *Aspergillis oryzae.*

Firstly, Boel et al teach a construction of a vector comprising a "TAKA-amylase promoter or functional parts thereof" for expression of a protein in Aspergillus (see especially abstract, lines 10-13). Boel et al further teach wherein the promoter contains a first base sequence "CCAATTAGAAG" and a second base sequence "CGGAAATTTAAAGG" that are arranged sequentially from the 5'-end side to the 3'-end side of said promoter (see especially sequence

of Figure 1, lines 17-19 and Boel et al claims 1-3). Boel et al teach the sequence "5'-ATTTAAAG-3'" which is upstream to the said first and second DNA sequences. Furthermore, Boel et al teach the modification of the *Aspergillis oryzae* taka-amylase promoter in the context of a vector expression system explicitly designed for expressing target proteins of interest for commercial protein production.

Therefore, Boel et al, in view of Minetoki et al, teach the modified promoter of claim 1, and further teach wherein said promoter capable of functioning in a filamentous fungus is a promoter of Taka-amylase of Aspergillus oryzae, which meets the limitations of claim 12. Furthermore, Boel et al teach a vector in which the modified promoter is integrated (claim 15) and a structural gene of a targeted protein is integrated under control of the modified promoter (claim 16) and further teaches wherein a transformed filamentous fungus comprises the vector and is capable of expressing said structural gene (claims 17-18), and producing a protein by culturing the filamentous fungus of claim 18 under conditions capable of producing protein; and collecting the produced protein (claim 19). For example, Boel et al recite "the gene for the desired product functionally linked to promoter and terminator sequences may be incorporated in a vector containing the selection marker' or may be placed on a separate vector or plasmid "capable of being integrated into the genome of the host strain" (col. 12, ¶ 1, lines 1-5). In addition, Boel et al teach the Taka-amylase promoter and collection of produced protein by accumulation of expressed protein in cells, followed by cell disruption,

or preferably, by collection of expressed proteins after proteins are secreted from host cells (col. 11, ¶ 2, lines 1-6 and abstract, lines 1-17 and Boel et al claim 5).

Therefore, Boel et al in combination with Minetonka et al meets all the limitations of claims 1-3, 7, 11-12, and 15-19.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have utilized the specific promoter sequences and vector system of Boel et al in the method taught in Minetoki *et al*. because Boel et al teach that the specific sequences and vector system was successfully used for expressing target genes in Aspergillus, was available, and was routine (e.g. col. 11, ¶ 2, lines 1-6 and abstract, lines 1-17 and Boel et al claim 5).

One would have been motivated at the time the invention was made to have utilized the SEQ ID NO: 3, 4 and 9 of Boel et al in the method of Minetoki because the Minetoki et al study particularly focuses on the modification and enhancement of the promoter regions of the three amylase-encoding genes *amyB* (also called taka-amylase or TAA), *glaA* and *agdA* of *Aspergillus oryzae* For example, Minetoki et al show motivation to explicitly use the sequences of the Taka-amylase promoter in the statement: "On the other hand, high-level expression signals, such as the *amyB* and *glaA* promoters, are frequently used for the overexpression of homologous and heterologous genes in a variety of filamentous fungi". Minetoki et al continue, "If high-level expression of *amyB* and *glaA* is dependent on region III, the insertion of region III into the promoter region could further elevate expression". Furthermore, Minetoki et al states that "In this study, multiple copies of the fragment comprising region III were introduced into

PagdA to enhance promoter activity and to determine the common regulatory mechanism for the repression of the *A.oryzae* amylase genes. The effect of introducing this fragment on gene expression is discussed. In addition, the merits of a conventional solid-state culture system of protein production are described". (e.g. abstract, lines 1-4; p.459, right column, lines 1-4; and p. 460, left column, ¶1-2). In addition, both Minetoki *et al*. and Boel *et al*. are in the same field of endeavor (promoter sequence construction) and both are directed to the same problem sought to be solved (enhanced promoters capable of use in a filamentous fungus).

Absent evidence to the contrary, one would have a reasonable expectation of success combining the teachings of the art because: the use of the SEQ ID NO: 3, 4 and 9 for the purpose of enhanced promoters capable of functioning in a filamentous fungus was successfully practiced by Boel *et al*. and are a species of the consensus sequences used by Minetoki et al (described in the instant claim 1); the use of the vector system of Boel et al was successfully used and was amenable to modifications (insertions, substitutions, deletions) of the promoter sequence as shown by the variations of promoter constructs reported in Boel et al; and the use of the specific Aspergillus orzae taka-amylase promoter was shown to be successfully used in Boel et al.

In view of the foregoing, the method of claims 1-3, 7, 11-12, and 15-19, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC *§103(a)*.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Catherine S. Hibbert, Ph.D., whose telephone number is 571-270-3053. The examiner can normally be reached on Monday-Friday, 7:30 AM-5:00 PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D., can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully submitted,
Catherine S. Hibbert
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/Daniel M Sullivan/
Primary Examiner, Art Unit 1636